Recovery from Severe Hyperthermia (45°C) and Rhabdomyolysis Induced by Methamphetamine Body-Stuffing

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INTRODUCTION

The acute toxic effects of sympathomimetic stimulant drugs include hypertensive crisis, coronary and cerebral vasospasm, cardiac dysrthythmias, seizures, hyperthermia, rhabdomyolysis, and metabolic derangements such as hyperglycemia, metabolic acidosis, and either hyper- or hypokalemia.[1] This report presents a case of complete recovery from severe hyperthermia with a temperature at 45°C (113°F) and rhabdomyolysis resulting from methamphetamine body-stuffing and physical exertion. The patient's initial recorded core body temperature is the highest ever reported in a case with laboratory-confirmed sympathomimetic drug overdose.

CASE REPORT

A 23-year-old man was a restrained driver involved in a minor motor vehicle collision with a police cruiser, and suffered no apparent injuries. Fearing that he would be arrested for possession of illicit drugs, the driver ingested what he later estimated to be 100 dose-units of methamphetamine (≥1 gram) he had been selling. He then fled the scene on foot. A chase ensued, and he was apprehended by police while running around the roof of one building and attempting to jump to another roof. The ambient temperature at that time was approximately 22°C (75°F), with a relative humidity of 39%, giving a heat index of 25°C (77°F). The police placed restraints on their suspect's lower extremities and then summoned paramedic-level emergency medical technicians (EMTs) to transport him for medical evaluation.

Upon their arrival, EMTs found the patient combative and screaming with a repetitive speech pattern. Vital signs in the field were: pulse at ~200/min (sinus tachycardia on cardiac monitor), respirations at 40/min (rapid and shallow), and an oxygen saturation of 98% on ambient air. Blood pressure could not be recorded due to the patient's agitation, and body temperature was not measured. Physical examination by the EMTs was notable for warm, diaphoretic skin, mydriasis, and some dried blood around the lips, but no other gross signs of trauma. Intravenous (IV) access could not be established due to the patient's agitation, and he was transported within 4 minutes to the nearest hospital emergency department (ED).

Upon arrival to the ED the patient was agitated, combative, and both physically and verbally threatening to the staff. He was placed in four-point leather restraints and rapidly evaluated. Vital signs were: pulse at 164/min, respirations at 30/min, blood pressure at 152/70 mmHg, and temperature at 43.6°C (110.4°F) orally. Only one oral temperature measurement was made before resuscitative measures began. IV access was established and hydration initiated with 0.9% saline in one-liter boluses. To control the patient's extreme agitation and facilitate treatment, he was endotracheally intubated with rapid sequence induction using 10 mg IV lorazepam and 10 mg IV vecuronium. A core body temperature was then measured at 45.0°C (113°F) with a rectal probe thermometer, which was used intermittently during the ED course. Additional cooling measures employed were the application of ice packs to the groin and axillae and a cooling blanket. A Foley catheter was inserted, with return of ~200cc dark, red urine. Physical examination revealed skin abrasions to the lower right anterior chest wall, bilateral knees and knuckles, apparently sustained during the chase, but no other evidence of trauma. An electrocardiogram revealed a wide-complex sinus tachycardia at a rate of 162/min with a QRS duration of 122 msec.

Initial laboratory results were: arterial pH at 7.38, pCO_2 at 31.0 mmHg, pO_2 at 551 mmHg, serum creatinine phosphokinase (CPK) at 2083 IU/L, CPK-MB at 10.9 IU/L, white blood cell count at 11.1 k/mm^3, hematocrit at 41.4%, and platelet count at 274 k/mm^3. Computed tomography of the head was within normal limits. Urine drug screening by enzyme-multiplied immunoassay technique (EMIT) was positive for amphetamines and cannabinoids only.

One hundred minutes after ED arrival, the patient's core temperature had decreased to 38.1°C (100.6°F). He was given a total of 6300cc IV fluids prior to transfer via helicopter to the regional toxicology referral center; urine output in this time was 1800cc over three hours.

The patient arrived in the intensive care unit (ICU) 3.5 hrs after initiation of treatment. Vital signs on ICU arrival were: temperature at 36.4°C (97.6°F), pulse at 128/min, and blood pressure at144/56 mmHg. Laboratory investigation showed: hematocrit at 37.9%, platelet count at 105 k/mm³, prothrombin time at 14.3 sec, fibrinogen at 258 mg/dL, fibrin split products at <5 mg/dL, sodium at 141 mEq/L, potassium at 3.8 mEq/L, chloride at 109 mEq/L, bicarbonate at 21 mEq/L, blood urea nitrogen (BUN) at 17 mg/dL, creatinine at 1.1 mg/dL, glucose at 112 mg/dL, calcium at 5.5 mEq/L, magnesium at 2.3 mEq/L, phosphate at 2.2 mEq/L, CPK at 12,173 IU/L, CPK-MB at 110 IU/L, with no detectable acetaminophen, salicylate, or ethanol. Comprehensive urine drug screening by EMIT, thin-layer chromatography (TLC), and gas chromatography-mass spectroscopy (GC-MS) confirmed the presence of methamphetamine, amphetamine, caffeine, and cannabinoids only. No cocaine or benzoylecgonine (the primary cocaine metabolite) were detected.

The patient was treated with supplemental IV calcium, and was given activated charcoal via nasogastric tube. Aggressive IV hydration with bicarbonate-containing fluids (D5W with 150 mEq NaHCO$_3$ and 40 mEq KCl per liter infused at 250 cc/hr) to alkalinize the urine was continued. Including the initial boluses with normal saline, the patient received 9200cc total IV fluids within the first 12 hours of treatment. A urinalysis performed 11 hours after ED arrival showed: pH at 9.0, specific gravity at 1.015, 3+ protein, 3+ blood, and 20-30 red blood cells/hpf.

The patient remained comatose for 26 hours after intubation, but was successfully extubated on the second hospital day. The patient exhibited tachycardia, agitation, confusion, picking movements of the hands, and paranoid delusional thinking which slowly resolved over the following two days. Serial laboratory measurements showed a rapid rise in serum CPK, peaking at 119,901 IU/L on the third hospital day. The patient's peak serum creatinine was 1.1 mg/dL (at the time of ICU admission), and the BUN peaked at 18 mg/dL a few hours later. The patient never developed clinical evidence for a compartment syndrome as the basis for his notable rhabdomyolysis, nor did he experience a drop in urine output. The patient was discharged home on hospital day 5, with serum CPK at 39,006 IU/L, BUN at 6 mg/dL, and creatinine at 0.7 mg/dL. The patient and his wife agreed that his mental status had returned to baseline, with no detectable neurologic deficits. The patient was advised to return immediately for decreased urinary output, weakness, or other problems.

DISCUSSION

Hyperthermia is well recognized as a cause of major morbidity and mortality.[2] Hyperthermia may be caused by environmental exposure, infection, central thermic dysregulation, and/or by ingestion of various drugs. During the period from 1999-2003, the Centers for Disease Control and Prevention reported 3,442 heat-related deaths in the United States, 2,239 of which were due to exposure to excessive environmental heat, but without documentation of hyperthermia in the victims. Of the remaining 1,203 deaths associated with hyperthermia, 345 (29%) were associated with "external causes (e.g., unintentional poisonings)".[3] The exact pathophysiologic cause of death from hyperthermia is not known, but is probably multifactorial. Autopsy results have shown tissue injury to the myocardium, kidneys, central nervous system, liver, and skeletal muscle. Tissue injury is often worse in cases of exertional heatstroke, compared to "classic" heatstroke due to excessive environmental exposure.[4]

In their review of 250 cases of drug-related heatstroke, Clark and Lipton found that nearly half of the patients had a maximal recorded body temperature of 40-41°C and their survival rate was 69%.[5] About one-quarter had a temperature of 41.1-42.1°C, with 53% survival; the remaining victims with temperatures >42.1°C had a survival rate of only 30%.[5] The highest reported core body temperature in a patient who survived without permanent residual deficits was 46.5°C (115.7°F).[6] This 52-year-old patient suffered from environmental heatstroke, possibly exacerbated by ethanol consumption. In fact, this patient's peak temperature was likely higher, as an accurate measurement was not made until 25 minutes after initiating active cooling measures.

A case of even more extreme hyperthermia from sympathomimetic drug use has been reported, but lacked positive laboratory test results to confirm the drug exposure. Roberts et al[7] reported the case of a patient with a rectal temperature of 45.6°C (114°F) after IV injection of a substance thought to be cocaine; however, no cocaine or amphetamines were detected in either blood or urine.

The extreme hyperthermia (45°C; 113°F) seen in the patient presented here, therefore, represents the highest reported core body temperature in a case with laboratory confirmation of psychostimulant drug exposure. Both the EMIT and GC-MS methodologies confirmed the presence of amphetamines and the absence of cocaine. The number of compounds that could be detected by GC-MS in the referral center's laboratory exceeded 1500, and included most anticholinergic drugs (such as atropine, scopolamine, diphenhydramine, benztropine, cyclic antidepressants, and antipsychotics) which might produce a similar clinical picture in overdose. These drug detection tests are qualitative, not quantitative, so they only prove drug exposure but not overdose. Serum

levels of methamphetamine and/or amphetamine would have been the most ideal laboratory confirmation of acute overdose, but these were not obtained during the period of the patient's acute, severe intoxication. Nevertheless, the patient's history and clinical course were consistent with acute, severe sympathomimetic toxicity.

Drug-related and combination drug/environmental heatstroke victims commonly develop multisystem organ failure, characterized by rhabdomyolysis, acute renal failure, and disseminated intravascular coagulation (DIC). The patient presented here never developed renal failure or DIC, despite extreme hyperthermia and severe rhabdomyolysis. Factors that may have affected outcome in this case include aggressive initial IV hydration, the relatively short duration of extreme hyperthermia, rapid employment of multiple cooling measures (including neuromuscular blockade), the patient's baseline good health, and other supportive care measures. Drug-related heatstroke patients may require unusually vigorous initial IV hydration to correct intravascular volume depletion and to ensure adequate renal blood flow and urine output, guarding against heme pigment-induced nephropathy.

CONCLUSION

Severe hyperthermia may occur from the combination of physical exertion and methamphetamine body-stuffing. Aggressive cooling measures, intravenous hydration, and urinary alkalinization resulted in complete recovery, despite rhabdomyolysis and prolonged sympathomimetic toxicity.

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